



General

Guideline Title

Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: U.S. Preventive Services Task Force recommendation statement.

Bibliographic Source(s)

U.S. Preventive Services Task Force (USPSTF). Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2014 Feb 18;160(4):271-81. [83 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: U.S. Preventive Services Task Force (USPSTF). Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement. *Ann Intern Med.* 2005 Sep 6;143(5):355-61.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The U.S. Preventive Services Task Force (USPSTF) grades its recommendations (A, B, C, D, or I) and identifies the levels of certainty regarding net benefit (High, Moderate, and Low). The definitions of these grades can be found at the end of the "Major Recommendations" field.

Summary of Recommendations and Evidence

The USPSTF recommends that primary care providers screen women who have family members with breast, ovarian, tubal, or peritoneal cancer with 1 of several screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in breast cancer susceptibility genes (*BRCA1* or *BRCA2*). Women with positive screening results should receive genetic counseling and, if indicated after counseling, BRCA testing. (B recommendation)

The USPSTF recommends against routine genetic counseling or BRCA testing for women whose family history is not associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes. (D recommendation)

Clinical Considerations

Patient Population Under Consideration

This recommendation applies to asymptomatic women who have not been diagnosed with BRCA-related cancer.

Women who have 1 or more family members with a known potentially harmful mutation in the *BRCA1* or *BRCA2* genes should be offered genetic counseling and testing.

The USPSTF recognizes the potential importance of further evaluating women who have a diagnosis of breast or ovarian cancer. Some women receive genetic testing as part of a cancer evaluation at the time of diagnosis of breast cancer. The USPSTF did not review the appropriate use of BRCA testing in the evaluation of women who are newly diagnosed with breast cancer. That assessment is part of disease management and is beyond the scope of this recommendation. Women who have been diagnosed with breast cancer in the past and who did not receive BRCA testing as part of their cancer care but have a family history of breast or ovarian cancer should be encouraged to discuss further evaluation with their clinician.

These recommendations do not apply to men, although male family members may be identified for testing during evaluation.

Family History Screening and Risk Assessment

Mutations in the BRCA genes cluster in families, exhibiting an autosomal dominant pattern of transmission in maternal or paternal lineage. During standard elicitation of family history information from patients, primary care providers should ask about specific types of cancer, primary cancer sites, which family members were affected, relatives with multiple types of primary cancer, and the age at diagnosis and sex of affected family members.

For women who have at least one family member with breast, ovarian, or other types of BRCA-related cancer, primary care providers may use one of several brief familial risk stratification tools to determine the need for in-depth genetic counseling.

Although several risk tools are available, those evaluated by the USPSTF include the Ontario Family History Assessment Tool, Manchester Scoring System, Referral Screening Tool, Pedigree Assessment Tool, and Family History Screen 7 (FHS-7) (see Tables 1 to 5 in the original guideline document). The Referral Screening Tool (an updated version, the B-RST, is available at www.breastcancergenescreen.org) and FHS-7 are the simplest and quickest to administer. All of these tools seem to be clinically useful predictors of which women should be referred for genetic counseling due to increased risk for potentially harmful BRCA mutations (most sensitivity estimates were >85%), although some models have been evaluated in only one study. To determine which patients would benefit from BRCA risk assessment, primary care providers should not use general breast cancer risk assessment models (for example, the National Cancer Institute Breast Cancer Risk Assessment Tool, which is based on the Gail model) because they are not designed to determine which women should receive genetic counseling or BRCA testing.

In general, these tools elicit information about factors that are associated with increased likelihood of BRCA mutations. Family history factors associated with increased likelihood of potentially harmful BRCA mutations include breast cancer diagnosis before age 50 years, bilateral breast cancer, presence of breast and ovarian cancer, presence of breast cancer in 1 or more male family members, multiple cases of breast cancer in the family, 1 or more family members with 2 primary types of BRCA-related cancer, and Ashkenazi Jewish ethnicity. The USPSTF recognizes that each risk assessment tool has limitations and found insufficient comparative evidence to recommend one tool over another. The USPSTF also found insufficient evidence to support a specific risk threshold for referral for testing.

Genetic Counseling

Genetic counseling about BRCA mutation testing may be done by trained health professionals, including trained primary care providers. Several professional organizations describe the skills and training necessary to provide comprehensive genetic counseling. The process of genetic counseling includes detailed kindred analysis and risk assessment for potentially harmful BRCA mutations; education about the possible results of testing and their implications; identification of affected family members who may be preferred candidates for testing; outlining options for screening, risk-reducing medications, or surgery for eligible patients; and follow-up counseling for interpretation of test results.

BRCA Mutation Testing

Adequate evidence suggests that current genetic sequencing tests can accurately detect BRCA mutations. Testing for BRCA mutations should be done only when an individual has a personal or family history that suggests an inherited cancer susceptibility, when an individual has access to a health professional who is trained to provide genetic counseling and interpret test results, and when test results will aid in decision making. Initial testing of a family member who has breast or ovarian cancer is the preferred strategy in most cases, but it is reasonable to test if no affected relative is available. It is essential that before testing, the individual is fully informed about the implications of testing and has expressed a desire for it.

The type of mutation analysis required depends on family history. Individuals from families with known mutations or from ethnic groups in which certain mutations are more common (for example, Ashkenazi Jewish women) can be tested for these specific mutations.

Individuals without linkages to families or groups with known mutations receive more comprehensive testing. In these cases, when possible, testing should begin with a relative who has breast or ovarian cancer to determine whether affected family members have a clinically significant mutation.

Tests for BRCA mutations are highly sensitive and specific for known mutations, but interpretation of results is complex and generally requires posttest counseling. Test results for genetic mutations are reported as positive (that is, potentially harmful mutation detected), variants of uncertain clinical significance, uninformative-negative, or true-negative. Women who have relatives with known BRCA mutations can be reassured about their inherited risk for a potentially harmful mutation if the results are negative (that is, a true-negative). Some studies suggest increased breast cancer risk in some women with true negative results. However, a comprehensive meta-analysis conducted for the USPSTF that included these studies found that breast cancer risk is generally not increased in women with true-negative results. An uninformative-negative result occurs when a woman's test does not detect a potentially harmful mutation but no relatives have been tested or no mutations have been detected in tested relatives. Available tests may not be able to identify mutations in these families. Risk for breast cancer is increased in women with uninformative-negative results.

Timing of Screening

Consideration of screening for potentially harmful BRCA mutations should begin once women have reached the age of consent (18 years). Primary care providers should periodically assess all patients for changes in family history (for example, comprehensive review at least every 5 to 10 years).

Interventions for Women Who Are BRCA Mutation Carriers

Interventions that may reduce risk for cancer or cancer-related death in women who are BRCA mutation carriers include earlier, more frequent, or intensive cancer screening; risk-reducing medications (for example, tamoxifen or raloxifene); and risk-reducing surgery (for example, mastectomy or salpingo-oophorectomy). However, the strength of evidence varies across the types of interventions.

Evidence is lacking on the effect of intensive screening for BRCA-related cancer on clinical outcomes in women who are BRCA mutation carriers. Medications, such as tamoxifen and raloxifene, have been shown to reduce the incidence of invasive breast cancer in high-risk women in the general population, but they have not been studied specifically in women who are BRCA mutation carriers.

In high-risk women and those who are BRCA mutation carriers, cohort studies of risk-reducing surgery (mastectomy and salpingo-oophorectomy) showed substantially reduced risk for breast or ovarian cancer. Breast cancer risk was reduced by 85% to 100% with mastectomy and by 37% to 100% with oophorectomy, and ovarian cancer risk was reduced by 69% to 100% with oophorectomy or salpingo-oophorectomy. Salpingo-oophorectomy was also associated with a 55% relative reduction in all-cause mortality (as measured during the course of the study) in women with BRCA1 or BRCA2 mutations and without a history of breast cancer.

Other Approaches to Prevention

The USPSTF recommendations on medications for breast cancer risk reduction are available on the [USPSTF Web site](#) . The USPSTF recommends against screening for ovarian cancer in women. This recommendation does not apply to women with known genetic mutations that increase their risk for ovarian cancer (for example, BRCA mutations).

Useful Resources

The National Cancer Institute Cancer Genetics Services Directory provides a list of professionals who offer services related to cancer genetics, including cancer risk assessment, genetic counseling, and genetic susceptibility testing (available at <http://www.cancer.gov/cancertopics/genetics/directory>).

Definitions:

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment	Offer/provide this service only if other considerations support offering or providing the service in an individual patient.

Grade	Grade Definitions	Suggestions for Practice
D	and patient preferences. There is at least moderate certainty that the net benefit is small. The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be measured.	Read "Clinical Considerations" section of USPSTF Recommendation Statement (see the "Major Recommendations" field). If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	<p>The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as:</p> <ul style="list-style-type: none"> • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice; and • Lack of coherence in the chain of evidence <p>As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.</p>
Low	<p>The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of:</p> <ul style="list-style-type: none"> • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice; and • A lack of information on important health outcomes <p>More information may allow an estimation of effects on health outcomes.</p>

Clinical Algorithm(s)

None available

Scope

Disease/Condition(s)

BRCA-related cancer, including:

- Breast cancer
- Ovarian cancer
- Tubal cancer

- Peritoneal cancer

Guideline Category

Counseling

Prevention

Risk Assessment

Screening

Clinical Specialty

Family Practice

Internal Medicine

Medical Genetics

Obstetrics and Gynecology

Oncology

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Nurses

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

- To assess the balance of the benefits and harms of risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women
- To evaluate and summarize research addressing specific key questions important to the USPSTF as it considers new recommendations for primary care practice

Target Population

Asymptomatic women who have not been diagnosed with BRCA-related cancer

Note: The target population includes women without cancer or known BRCA mutations who are seen in clinical settings applicable to U.S. primary care practice, although the ideal candidate for mutation testing could be a male or female relative with cancer.

Interventions and Practices Considered

1. Family history
2. Screening for women with increased risk for potentially harmful BRCA mutations
3. Genetic counseling
4. BRCA testing

Note: Routine genetic counseling or BRCA testing is not recommended.

Major Outcomes Considered

- Key Question 1: Do risk assessment, genetic counseling, and genetic testing lead to reduced incidence of BRCA-related cancer and reduced cause-specific and all-cause mortality?
- Key Question 2a: What is the accuracy of methods to assess familial cancer risk for BRCA-related cancer when performed by a nonspecialist in genetics in a clinical setting?
- Key Question 2b: What are the benefits of genetic counseling in determining eligibility for genetic testing for BRCA-related cancer?
- Key Question 2c: Among women with increased risk for BRCA-related cancer what is the clinical validity of genetic testing for deleterious mutations?
- Key Question 3: What are the potential adverse effects of a) risk assessment, b) genetic counseling, and c) genetic testing?
- Key Question 4: Do interventions reduce the incidence of BRCA-related cancer and mortality in women with increased risk?
- Key Question 5: What are the potential adverse effects of interventions to reduce risk for BRCA-related cancer?

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was prepared by the Pacific Northwest Evidence-based Practice Center (EPC) and Oregon Health & Science University for the U.S. Preventive Services Task Force (USPSTF) (see the "Availability of Companion Documents" field).

Data Sources

The EPC staff searched MEDLINE from 2004 to 31 December 2012, the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews from 2005 through the fourth quarter of 2012, and Health Technology Assessment during the fourth quarter of 2012 for relevant English-language studies, systematic reviews, and meta-analyses. They manually reviewed reference lists of articles and reviewed citations of key studies by using Scopus.

Study Selection

Research published in 2003 or later and done in the United States or in populations that receive services and interventions applicable to medical practice in the United States was reviewed. Randomized, controlled trials (RCTs); systematic reviews; prospective and retrospective cohort studies; case-control studies; and diagnostic accuracy evaluations were included if they addressed the accuracy of risk assessment methods, outcomes of genetic counseling and testing, and the effectiveness of interventions to reduce BRCA-related cancer and mortality among mutation carriers.

Risk assessment methods were included if they were designed to guide referrals to genetic counselors or other genetic specialists and were usable by nonspecialists in genetics in clinical settings (that is, methods that were brief and nontechnical and did not require special training to administer or interpret). Evaluation of comprehensive models used in the practice of genetic counseling was outside the scope of this review, which focuses on

primary care practice. Interventions included intensive screening, risk reducing medications, and risk-reducing surgery. Only risk-reducing medications approved by the U.S. Food and Drug Administration (that is, tamoxifen and raloxifene) were considered, consistent with the scope of the USPSTF.

Studies of any design were included if they described potential adverse effects, including inaccurate risk assessment; inappropriate testing; false-positive and false negative results; false reassurance; incomplete testing; misinterpretation of results; anxiety; cancer-related worry; immediate and long-term harms associated with interventions; and ethical, legal, and social implications. For adverse effects of interventions, studies were included that enrolled women at high risk for BRCA-related cancer regardless of their mutation status.

After an initial review of abstracts, the EPC staff reviewed full-text articles by using additional inclusion criteria. Studies from the prior review that met inclusion criteria for the update were included to build on previous relevant research. Appendix Figure 2 in the original guideline document shows the results of the search and selection process.

Number of Source Documents

- Accuracy of risk assessment: 10
- Benefits and harms of genetic counseling: 27
- Harms of genetic testing: 14
- Effectiveness of interventions: 7
- Harms of interventions: 15

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Weighting According to a Rating Scheme (Scheme Not Given)

Rating Scheme for the Strength of the Evidence

Not stated

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was prepared by the Pacific Northwest Evidence-based Practice Center (EPC) and Oregon Health & Science University for the U.S. Preventive Services Task Force (USPSTF) (see the "Availability of Companion Documents" field).

Data Abstraction and Quality Assessment

An investigator abstracted data about the study design and setting; participant characteristics; procedures for data collection; number of participants enrolled and lost to follow-up; methods of exposure and outcome ascertainment; analytic methods, including adjustment for confounders; and outcomes. A second investigator confirmed the accuracy of key data. Two investigators used predefined criteria for RCTs; systematic reviews; and cohort, case-control, and diagnostic accuracy studies developed by the USPSTF to rate the quality of studies (good, fair, or poor) and resolved discrepancies by consensus.

Quality could not be assessed for many studies with designs that did not have predefined criteria, such as descriptive, cross-sectional, and pre-post studies, and case series. The applicability of studies was determined using the population, intervention, comparator, outcomes, timing of outcomes measurement, and setting format adapted to this topic.

Because of heterogeneity across studies, results were not combined in a quantitative meta-analysis. The EPC staff assessed the aggregate quality of the body of evidence (good, fair, or poor) by using methods that the USPSTF developed on the basis of the number, quality, and size of studies and consistency of results between studies. Studies were considered consistent if outcomes were generally in the same direction of effect and ranges of effect sizes were narrow.

Methods Used to Formulate the Recommendations

Balance Sheets

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The U.S. Preventive Services Task Force (USPSTF) systematically reviews the evidence concerning both the benefits and harms of widespread implementation of a preventive service. It then assesses the certainty of the evidence and the magnitude of the benefits and harms. On the basis of this assessment, the USPSTF assigns a letter grade to each preventive service signifying its recommendation about provision of the service (see Table below). An important, but often challenging, step is determining the balance between benefits and harms to estimate "net benefit" (that is, benefits minus harms).

Table 1. U.S. Preventive Services Task Force Recommendation Grid*

Certainty of Net Benefit	Magnitude of Net Benefit			
	Substantial	Moderate	Small	Zero/Negative
High	A	B	C	D
Moderate	B	B	C	D
Low	Insufficient			

*A, B, C, D, and I (*Insufficient*) represent the letter grades of recommendation or statement of insufficient evidence assigned by the USPSTF after assessing certainty and magnitude of net benefit of the service (see the "Rating Scheme for the Strength of the Recommendations" field).

The overarching question that the USPSTF seeks to answer for every preventive service is whether evidence suggests that provision of the service would improve health outcomes if implemented in a general primary care population. For screening topics, this standard could be met by a large randomized, controlled trial (RCT) in a representative asymptomatic population with follow-up of all members of both the group "invited for screening" and the group "not invited for screening."

Direct RCT evidence about screening is often unavailable, so the USPSTF considers indirect evidence. To guide its selection of indirect evidence, the USPSTF constructs a "chain of evidence" within an analytic framework. For each key question, the body of pertinent literature is critically appraised, focusing on the following 6 questions:

1. Do the studies have the appropriate research design to answer the key question(s)?
2. To what extent are the existing studies of high quality? (i.e., what is the internal validity?)
3. To what extent are the results of the studies generalizable to the general U.S. primary care population and situation? (i.e., what is the external validity?)
4. How many studies have been conducted that address the key question(s)? How large are the studies? (i.e., what is the precision of the evidence?)
5. How consistent are the results of the studies?
6. Are there additional factors that assist the USPSTF in drawing conclusions (e.g., presence or absence of dose–response effects, fit within a biologic model)?

The next step in the USPSTF process is to use the evidence from the key questions to assess whether there would be net benefit if the service were implemented. In 2001, the USPSTF published an article that documented its systematic processes of evidence evaluation and recommendation development. At that time, the USPSTF's overall assessment of evidence was described as good, fair, or poor. The USPSTF

realized that this rating seemed to apply only to how well studies were conducted and did not fully capture all of the issues that go into an overall assessment of the evidence about net benefit. To avoid confusion, the USPSTF has changed its terminology. Whereas individual study quality will continue to be characterized as good, fair, or poor, the term certainty will now be used to describe the USPSTF's assessment of the overall body of evidence about net benefit of a preventive service and the likelihood that the assessment is correct. Certainty will be determined by considering all 6 questions listed above; the judgment about certainty will be described as high, moderate, or low.

In making its assessment of certainty about net benefit, the evaluation of the evidence from each key question plays a primary role. It is important to note that the USPSTF makes recommendations for real-world medical practice in the United States and must determine to what extent the evidence for each key question—even evidence from screening RCTs or treatment RCTs—can be applied to the general primary care population. Frequently, studies are conducted in highly selected populations under special conditions. The USPSTF must consider differences between the general primary care population and the populations studied in RCTs and make judgments about the likelihood of observing the same effect in actual practice.

It is also important to note that one of the key questions in the analytic framework refers to the potential harms of the preventive service. The USPSTF considers the evidence about the benefits and harms of preventive services separately and equally. Data about harms are often obtained from observational studies because harms observed in RCTs may not be representative of those found in usual practice and because some harms are not completely measured and reported in RCTs.

Putting the body of evidence for all key questions together as a chain, the USPSTF assesses the certainty of net benefit of a preventive service by asking the 6 major questions listed above. The USPSTF would rate a body of convincing evidence about the benefits of a service that, for example, derives from several RCTs of screening in which the estimate of benefits can be generalized to the general primary care population as "high" certainty (see the "Rating Scheme for the Strength of the Recommendations" field). The USPSTF would rate a body of evidence that was not clearly applicable to general practice or has other defects in quality, research design, or consistency of studies as "moderate" certainty. Certainty is "low" when, for example, there are gaps in the evidence linking parts of the analytic framework, when evidence to determine the harms of treatment is unavailable, or when evidence about the benefits of treatment is insufficient. Table 4 in the methodology document listed below (see the "Availability of Companion Documents" field) summarizes the current terminology used by the USPSTF to describe the critical assessment of evidence at all 3 levels: individual studies, key questions, and overall certainty of net benefit of the preventive service.

Sawaya GF, Guirguis-Blake J, LeFevre M, Harris R, Petitti D; U.S. Preventive Services Task Force. Update on the methods of the U.S. Preventive Services Task Force: estimating certainty and magnitude of net benefit. *Ann Intern Med*. 2007;147(12):871-5. [5 references].

Rating Scheme for the Strength of the Recommendations

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

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B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer/provide this service only if other considerations support offering or providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be measured.	Read "Clinical Considerations" section of USPSTF Recommendation Statement (see the "Major Recommendations" field). If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Definition: The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	<p>The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as:</p> <ul style="list-style-type: none"> • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice; and • Lack of coherence in the chain of evidence <p>As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.</p>
Low	<p>The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of:</p> <ul style="list-style-type: none"> • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice; and • A lack of information on important health outcomes <p>More information may allow an estimation of effects on health outcomes.</p>

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Comparison with Guidelines from Other Groups

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Peer Review. Before the U.S. Preventive Services Task Force (USPSTF) makes its final determinations about recommendations on a given preventive service, the Evidence-based Practice Center and the Agency for Healthcare Research and Quality send a draft evidence review to 4 to 6 external experts and to Federal agencies and professional and disease-based health organizations with interests in the topic. The experts are asked to examine the review critically for accuracy and completeness and to respond to a series of specific questions about the document. After assembling these external review comments and documenting the proposed response to key comments, the topic team presents this information to the USPSTF in memo form. In this way, the USPSTF can consider these external comments before it votes on its recommendations about the service. Draft recommendation statements are then circulated for comment among reviewers representing professional societies, voluntary organizations, and Federal agencies, as well as posted on the USPSTF Web site for public comment. These comments are discussed before the final recommendations are confirmed.

Response to Public Comment. A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 2 April through 29 April 2013. In response to comments, the USPSTF clarified that this recommendation statement applies to women. It also

expanded the recommendation to include women who have family members with tubal or peritoneal (in addition to breast or ovarian) cancer. The USPSTF clarified that it recognizes the potential importance of further evaluating women who have a diagnosis of breast or ovarian cancer; however, that assessment is part of disease management and is beyond the scope of this recommendation.

The USPSTF added that it found insufficient evidence to recommend one risk assessment tool over another or to support a specific risk threshold for referral for genetic counseling and BRCA testing. It also added a compilation of risk assessment tools (see Tables 1 to 5 in the original guideline document). Although the preferred BRCA testing strategy is initial testing of a family member with breast or ovarian cancer, the USPSTF clarified that it is reasonable to start testing in an unaffected individual if no affected relative is available. Because of the complexity of BRCA test results, the USPSTF also suggests posttest counseling. It also clarified and updated information on BRCA testing, other resources, and recommendations of other groups.

Recommendations of Others. Recommendations for screening from the following groups were discussed: National Comprehensive Cancer Network; American Congress of Obstetricians and Gynecologists (ACOG); American Society of Clinical Oncology (ASCO); American Society of Human Genetics; National Society of Genetic Counselors; European Society for Medical Oncology; and Society of Gynecologic Oncologists.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Benefits of Testing for Potentially Harmful BRCA Mutations

- For women whose family history is associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes, adequate evidence suggests that the benefits of testing for potentially harmful BRCA mutations are moderate.
- For women whose family history is not associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes, there is adequate evidence that the benefits of testing for potentially harmful BRCA mutations are few to none.

Potential Harms

Harms of Detection of Potentially Harmful BRCA Mutations and Early Intervention and Treatment

Adequate evidence suggests that the overall harms of detection of and early intervention for potentially harmful BRCA mutations are small to moderate.

Qualifying Statements

Qualifying Statements

- The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific clinical preventive services for patients without related signs or symptoms.
- It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.
- The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

- Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Implementation of the Guideline

Description of Implementation Strategy

The experiences of the first and second U.S. Preventive Services Task Force (USPSTF), as well as that of other evidence-based guideline efforts, have highlighted the importance of identifying effective ways to implement clinical recommendations. Practice guidelines are relatively weak tools for changing clinical practice when used in isolation. To effect change, guidelines must be coupled with strategies to improve their acceptance and feasibility. Such strategies include enlisting the support of local opinion leaders, using reminder systems for clinicians and patients, adopting standing orders, and audit and feedback of information to clinicians about their compliance with recommended practice.

In the case of preventive services guidelines, implementation needs to go beyond traditional dissemination and promotion efforts to recognize the added patient and clinician barriers that affect preventive care. These include clinicians' ambivalence about whether preventive medicine is part of their job, the psychological and practical challenges that patients face in changing behaviors, lack of access to health care or of insurance coverage for preventive services for some patients, competing pressures within the context of shorter office visits, and the lack of organized systems in most practices to ensure the delivery of recommended preventive care.

Dissemination strategies have changed dramatically in this age of electronic information. While recognizing the continuing value of journals and other print formats for dissemination, the USPSTF will make all its products available through its [Web site](#) . The combination of electronic access and extensive material in the public domain should make it easier for a broad audience of users to access USPSTF materials and adapt them for their local needs. Online access to USPSTF products also opens up new possibilities for the appearance of the annual, pocket-size *Guide to Clinical Preventive Services*.

To be successful, approaches for implementing prevention have to be tailored to the local level and deal with the specific barriers at a given site, typically requiring the redesign of systems of care. Such a systems approach to prevention has had notable success in established staff-model health maintenance organizations, by addressing organization of care, emphasizing a philosophy of prevention, and altering the training and incentives for clinicians. Staff-model plans also benefit from integrated information systems that can track the use of needed services and generate automatic reminders aimed at patients and clinicians, some of the most consistently successful interventions. Information systems remain a major challenge for individual clinicians' offices, however, as well as for looser affiliations of practices in network-model managed care and independent practice associations, where data on patient visits, referrals, and test results are not always centralized.

Implementation Tools

Foreign Language Translations

Mobile Device Resources

Patient Resources

Pocket Guide/Reference Cards

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

U.S. Preventive Services Task Force (USPSTF). Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2014 Feb 18;160(4):271-81. [83 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1996 (revised 2014 Feb 18)

Guideline Developer(s)

U.S. Preventive Services Task Force - Independent Expert Panel

Guideline Developer Comment

The U.S. Preventive Services Task Force (USPSTF) is a federally-appointed panel of independent experts. Conclusions of the USPSTF do not necessarily reflect policy of the U.S. Department of Health and Human Services (DHHS) or its agencies.

Source(s) of Funding

The U.S. Preventive Services Task Force (USPSTF) is an independent, voluntary body. The U.S. Congress mandates that the Agency for Healthcare Research and Quality support the operations of the USPSTF.

Guideline Committee

U.S. Preventive Services Task Force (USPSTF)

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Financial Disclosures/Conflicts of Interest

The U.S. Preventive Services Task Force (USPSTF) has an explicit policy concerning conflict of interest. All members disclose at each meeting if they have a significant financial, professional/business, or intellectual conflict for each topic being discussed. USPSTF members with conflicts may be recused from discussing or voting on recommendations about the topic in question.

Potential Conflict of Interest: Disclosure forms from USPSTF members can be viewed at <https://www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M13-2747> .

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: U.S. Preventive Services Task Force (USPSTF). Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement. *Ann Intern Med.* 2005 Sep 6;143(5):355-61.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the [Annals of Internal Medicine Web site](#) .

Availability of Companion Documents

The following are available:

Evidence Reviews:

- Nelson HD, Pappas M, Zakher B, Mitchell JP, Okinaka-Hu L, Fu R. Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: a systematic review to update the U.S. Preventive Services Task Force recommendation. *Ann Intern Med.* 2014;160(4):255-66.
- Nelson HD, Fu R, Goddard K, Mitchell JP, Okinaka-Hu L, Pappas M, Zakher B. Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer: systematic review to update the U.S. Preventive Services Task Force Recommendation. Evidence Synthesis No. 101. AHRQ Publication No. 12-05164-EF-1. Rockville (MD): Agency for Healthcare Research and Quality; 2013 Dec. 366 p.

Electronic copies: Available from the [U.S. Preventive Services Task Force \(USPSTF\) Web site](#) .

Background Articles:

- Barton MB et al. How to read the new recommendation statement: methods update from the U.S. Preventive Services Task Force. *Ann Intern Med* 2007;147:123-127.
- Guirguis-Blake J et al. Current processes of the U.S. Preventive Services Task Force: refining evidence-based recommendation development. *Ann Intern Med* 2007;147:117-122.

- Sawaya GF et al. Update on the methods of the U.S. Preventive Services Task Force: estimating certainty and magnitude of net benefit. *Ann Intern Med* 2007;147:871-875.

Electronic copies: Available from the [USPSTF Web site](#) .

The following is also available:

- Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women. Clinical summary of U.S. Preventive Services Task Force Recommendation. 2014. 1 p. Electronic copies: Available from the [USPSTF Web site](#) .
- Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer. USPSTF Final research plan. Electronic copies: Available from the [USPSTF Web site](#) .
- The guide to clinical preventive services, 2012. Recommendations of the U.S. Preventive Services Task Force. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ), 2012. 128 p. Electronic copies: Available from the [AHRQ Web site](#) . See the related QualityTool summary on the [Health Care Innovations Exchange Web site](#) .
- A continuing medical education (CME) is available from the [Annals of Internal Medicine Web site](#) .

The [Electronic Preventive Services Selector \(ePSS\)](#) is an application designed to provide primary care clinicians and health care teams timely decision support regarding appropriate screening, counseling, and preventive services for their patients. It is based on the current, evidence-based recommendations of the USPSTF and can be searched by specific patient characteristics, such as age, sex, and selected behavioral risk factors.

Patient Resources

The following are available:

- Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women. Understanding task force recommendations. Rockville (MD): U.S. Preventive Services Task Force. Consumer fact sheet. 2013 Dec. 6 p. Electronic copies: Available from the [U.S. Preventive Services Task Force \(USPSTF\) Web site](#) .
- Assessing the genetic risk for BRCA-related breast or ovarian cancer in women: recommendations from the U.S. Preventive Services Task Force. Summaries for patients. *Ann Intern Med*. 2014;160(4):I-16-16. Electronic copies: Available from the [Annals of Internal Medicine Web site](#) .
- Women: stay healthy at any age. Rockville (MD): Agency for Healthcare Research and Quality. AHRQ Pub. No. 10-IP002-A. 2010 Aug. 2 p. Electronic copies: Available in Portable Document Format (PDF) in [English](#) and [Spanish](#) from the AHRQ Web site. See the related QualityTool summary on the [Health Care Innovations Exchange Web site](#) .

Print copies: Available in English and Spanish from the Agency for Healthcare Research and Quality (AHRQ) Publications Clearinghouse. For more information, go to <http://www.ahrq.gov/research/publications/index.html> or call 1-800-358-9295 (U.S. only).

Myhealthfinder is a tool that provides personalized recommendations for clinical preventive services specific to the user's age, gender, and pregnancy status. It features evidence-based recommendations from the USPSTF and is available at www.healthfinder.gov

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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